

Case Report

Metallo- β -lactamase-producing *Klebsiella pneumoniae* infection in a non-hospital environment

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Case: A 92-year-old female resident at a nursing home was transported to the emergency department unconscious, hypotensive, and febrile. Chest X-rays and computed tomography revealed a permeation shadow in the right lung. The patient was diagnosed with sepsis due to pneumonia. At the time of admission, she had not received antibiotics or treatment using medical devices over the past 6 months. Two sets of samples were taken for blood and sputum cultures, and *Klebsiella pneumoniae* was isolated from all cultures. The strain was identified as metallo- β -lactamase-producing *K. pneumoniae*, and the patient was successfully treated with tazobactam-piperacillin. This case indicates that metallo- β -lactamase-producing *K. pneumoniae* infection occurred in a non-hospital environment.

Outcome: After tazobactam-piperacillin treatment, the patient was transferred to another hospital.

Conclusion: Emergency physicians should be aware of multidrug-resistant bacterial infection even in a non-hospital setting.

Key words: Community-acquired infection, extended-spectrum β -lactamases (ESBLs), *Klebsiella pneumoniae*, metallo- β -lactamase (MBL), sepsis

INTRODUCTION

IN JAPAN, THE detection rate of multidrug-resistant gram-negative bacteria such as plasmid-mediated extended-spectrum β -lactamase (ESBL)-producing *Klebsiella pneumoniae* is gradually increasing in hospitals and community settings.^{1–3} Community-acquired infections due to ESBL-producing *Escherichia coli* and *K. pneumoniae* are becoming a major concern for outpatients due to the inappropriate use of empirical antibiotics, such as cephalosporins and fluoroquinolones. The increase in community-acquired ESBL-producing *E. coli* and *K. pneumoniae* infection is compelling us to use carbapenems.^{2–4} The use of carbapenems or β -lactam antibiotics is a risk factor for metallo- β -lactamase (MBL)-producing gram-negative bacterial infections.⁵ The

identification of carbapenemase-producing *E. coli* and *K. pneumoniae* strains is reported as evidence for additional β -lactamase-producing bacteria other than ESBL-producing bacteria.⁶ Thus, emergency physicians should pay attention to MBL-producing gram-negative bacterial infections in community settings as well as hospital settings.

We report the first case of sepsis in Gunma Prefecture due to pneumonia caused by MBL-producing *K. pneumoniae* infection acquired at a nursing home. This case highlights the spread of MBL-producing organisms in social environments in Japan.

CASE

A 92-YEAR-OLD FEMALE RESIDENT at a nursing home was transported to the emergency department of the Gunma University Hospital (Maebashi, Japan) in a state of impaired unconsciousness and hypotension. The day before hospitalization, she developed fever and weakness. Her medical and family histories were unavailable. Moreover, she had not received any treatment or antibiotics within the 6 months prior to her admission.

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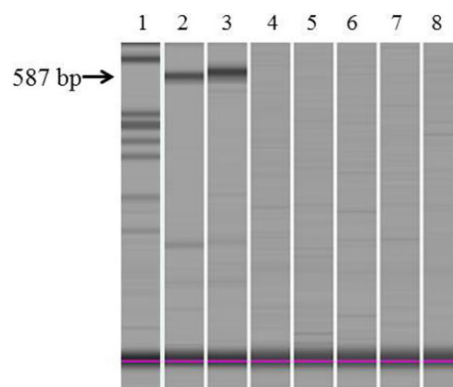
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Table 1. Antimicrobial susceptibility testing of *Klebsiella pneumoniae*

	Minimum inhibitory concentration, µg/mL
Ampicillin	>16
Piperacillin	>64
Piperacillin/tazobactam	≤16
Cefazolin	>16
Cefotiam	>16
Cefotaxime	>32
Ceftazidime	>16
Cefpirome	≤8
Cefaclor	>16
Cefpodoxime	>4
Cefcapene	>1
Cefmetazole	>32
Flomoxef	>32
Imipenem	4
Aztreonam	≤8
Amoxicillin/clavulanate	>16
Sulbactam/cefoperazone	>32
Gentamicin	2
Amikacin	≤4
Minocycline	>8
Levofloxacin	≤1
Sulfamethoxazole/trimethoprim	≤2
Fosfomycin	16

At the time of admission, her vital signs were: Glasgow Coma Scale, E3V3M6; blood pressure, 65/35 mmHg; pulse rate, irregular at 115 b.p.m.; respiratory rate, 25/min; peripheral oxygen saturation, 87% (O₂; 8 L/min); and body temperature, 38.0°C. The blood test results were: white blood cell count, 4,800/µL; C-reactive protein level, 1.8 mg/L; and procalcitonin level, 7.6 ng/mL. Chest X-rays and computed tomography revealed a permeation shadow in the right lung. The patient was diagnosed with sepsis due to pneumonia and was subsequently treated with dopamine.

Two sets of samples were taken for blood and sputum cultures, and *K. pneumoniae* was isolated from all cultures. Thereafter, the patient was treated with tazobactam–piperacillin. The test results of antibacterial drug sensitivity for *K. pneumoniae* are shown in Table 1. The minimum inhibitory concentration of cephalosporins and cephamycins against *K. pneumoniae* suggested that this strain of *K. pneumoniae* produced ESBL and/or carbapenemase. The strain of *K. pneumoniae* isolated from the patient was negative for the standard ESBL identification test, namely the ESBL plus test (Siemens, Tokyo, Japan) and the Etest

**Fig. 1.** Polymerase chain reaction analysis of the *Klebsiella pneumoniae* strain. Lane 1, marker; lane 2, positive control (587 bp); lanes 3–5, *K. pneumoniae* metallo-β-lactamases: lane 3, IMP-1; lane 4, IMP-2; lane 5, VIM-2; lane 6, *K. pneumoniae* carbapenemase; lane 7, negative control.

(Sysmex bioMérieux, Tokyo, Japan). The isolate was also negative for the boronic acid identification test for class C-β-lactamase producing *K. pneumoniae*.⁷ However, the isolate was positive for the modified Hodge test of carbapenemase production. A simple disk diffusion test using thiol compounds for the detection of IMP-1-type MBL-producing gram-negative bacteria,⁸ as well as polymerase chain reaction analysis using bla-IMP-specific primers,^{8,9} revealed that the *K. pneumoniae* strain was an IMP-1-type MBL (Fig. 1).

The patient received life support treatment according to Surviving Sepsis Campaign Guidelines 2012 and the infection was treated by tazobactam–piperacillin. Thereafter, the general condition of the patient recovered, as described in Table 2. On the sixth hospital day, she was transferred to another hospital for continuation of treatment.

DISCUSSION

THIS PATIENT WAS the first reported case of sepsis due to pneumonia caused by MBL-producing *K. pneumoniae* acquired at a nursing home. In addition, this is the first strain of MBL-producing *K. pneumoniae*-causing infection that was isolated at Gunma University Hospital. This case suggests that MBL-producing *K. pneumoniae* might be spreading in social environments, including nursing homes.

Reports of infections with MBL-producing gram-negative bacteria are increasing worldwide,¹⁰ with IMP-1 and VIM-2 as the predominant MBLs in Japan.⁹ The carrier rate of clinically isolated MBL-producing *K. pneumoniae* strains was low (<2.3%) in Japanese hospitals.^{5,11} MBL-producing

Table 2. Vital signs and blood test results of this case

	Day 1	Day 2	Day 6
Body temperature (°C)	38	37.7	37.1
White blood cell count (/μL)	4,800	12,100	8,300
C reactive protein (mg/dL)	17.96	27.59	5.11
Peripheral oxygen saturation	87% (O ₂ 8 L/min)	95% (O ₂ 8 L/min)	97% (O ₂ 4 L/min)
Dopamine hydrochloride (μg/kg/min)	10	10	7

Table 3. Carrier rate of extended-spectrum β-lactamase (ESBL)- or metallo-β-lactamase (MBL)- producing *Klebsiella pneumoniae* at Gunma University Hospital (Maebashi, Japan)

Year	2010	2011	2012	2013	Total (2010–2013)
No. of clinically isolated <i>K. pneumoniae</i>	148	122	148	146	564
No. of ESBL-producing <i>K. pneumoniae</i> (carrier rate, %)	15 (10.1)	9 (7.4)	5 (3.4)	5 (3.4)	34 (6.0)
No. of MBL-producing <i>K. pneumoniae</i> (carrier rate, %)	0 (0)	0 (0)	0 (0)	1 [†] (0.7)	1 [†] (0.2)

†Case reported in this article.

K. pneumoniae infections are reported to be sporadic and the prevalence is increasing in Japanese hospitals.^{5,11} The risk factors for MBL-producing bacterial infection include the administration of carbapenems or β-lactam antibiotics, hospitalization and/or procedures with infected indwelling medical devices.^{5,9,10} In Japan, the detection rate of ESBL-producing *K. pneumoniae* is gradually increasing in hospitals and community settings.^{2,3} The increase in the number of patients infected with ESBL-producing gram-negative bacteria has led to the widespread use of carbapenems. In the present case, the patient was elderly, but her health status was stable at the nursing home. The day before hospitalization, she had a fever and loss of vigor, and she did not receive any treatment for these symptoms. She did not receive any antibiotics within the 6 months prior to her admission to our hospital. Furthermore, the patient was admitted to Gunma University Hospital during a period of steady decrease in the carrier rate for ESBL-producing *K. pneumoniae* (Table 3). At Gunma University Hospital, the carrier rate of ESBL-producing *K. pneumoniae* decreased from 10.1% in 2010 to 3.4% in 2013, and we never detected a strain of MBL-producing *K. pneumoniae*, except this case, during this period. Our observations suggest that MBL-producing pathogens are spreading in healthcare-associated environments, such as nursing homes. Altogether, these data suggest that MBL-producing *K. pneumoniae* infection is a healthcare-associated infection at the nursing home.

In conclusion, we report a case of MBL-producing *K. pneumoniae* infection in a patient residing at a nursing home. The restricted use of antibiotics, strict hygiene practices, and rapid detection of these strains are important to minimize the prevalence of these drug-resistant strains in clinical and social environments. Emergency physicians should be aware of multidrug-resistant bacterial infection, even in a non-hospital setting.

CONFLICT OF INTEREST

NONE.

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